UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

UNITED STATES OF AMERICA	)	Criminal No. 18cr10461
v.	)	Violation:
ev3, INC.,	)	Count One: Introduction into Interstate Commerce of Adulterated Medical Devices
Defendant	)	21 U.S.C. §§ 331(a), 333(a)(1)
	)	Forfeiture Allegation:
	)	18 U.S.C. § 982(a)(7), 28 U.S.C. § 2461(c),
	)	21 U.S.C. §§ 334 and 853(p)

INFORMATION

At all times material to this Information:

The Defendant

1. ev3, Inc. ("ev3"), was a Delaware corporation that made and manufactured medical devices used in the treatment of vascular diseases. It had a principal place of business in Plymouth, Minnesota. In November 2005, ev3 acquired a medical device manufacturer called Micro Therapeutics, Inc. ("MTI"), with its principal place of business in Irvine, California. MTI became the neurovascular division of ev3. ev3 manufactured and distributed in interstate commerce, in the District of Massachusetts and elsewhere, medical devices intended for human use.

The Food and Drug Administration and the Food, Drug & Cosmetic Act

2. The United States Food and Drug Administration ("FDA") was an agency of the United States responsible for protecting the health and safety of the public by assuring that, among other things, medical devices intended for use in humans were safe and effective for their intended uses. The FDA regulated the manufacture, labeling, and shipment in interstate commerce of medical devices through enforcement of the Food, Drug, and Cosmetic Act

("FDCA"). One of the purposes of the FDCA was to ensure that medical devices sold for human use are safe and effective.

3. The FDCA defined a medical device, in relevant part, as "an instrument, apparatus, implement, machine, contrivance, implant, in vitro agent, or other similar or related article, including any component, part, or accessory, which is . . . intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals. . . ." 21 U.S.C. § 321(h).

4. Under the FDCA, the term "labeling" was defined as all labels and other printed or graphic matter upon any article, including medical devices, or any of its containers or wrappers, or accompanying such articles. 21 U.S.C. § 321(m).

5. The FDCA and its implementing regulations prohibited manufacturers from distributing in interstate commerce any medical device for an intended use unless the FDA had granted marketing approval for that use of the device or the device was covered by an exemption not applicable here.

6. The manufacturer could lawfully distribute a medical device for an intended use by obtaining FDA approval of the manufacturer's application for premarket approval ("PMA"). The FDA would grant PMA approval only if the information in the PMA provided FDA with reasonable assurance that the device was safe and effective when used according to its FDA-approved labeling for its intended use. 21 U.S.C. § 360e(d). The approved intended use would be reflected in the FDA-approved labeling accompanying the device.

7. Under the FDCA, a device was "adulterated" if it lacked a premarket approval for a use intended by the manufacturer, unless an exception not relevant here applied. 21 U.S.C. § 351(f)(1)(B). A medical device's "intended use" included the "objective intent of the persons legally responsible for the labeling of devices," which could be demonstrated by, among other

things, evidence concerning "oral or written statements by such persons or their representatives" and "the circumstances that the article [was], with the knowledge of such persons or their representatives, offered and used for a purpose for which it [was] neither labeled nor advertised." 21 C.F.R. § 801.4.

8. The FDCA prohibited the introduction or delivery for introduction into interstate commerce of an adulterated device. 21 U.S.C. § 331(a).

The Onyx Medical Device

9. The Onyx Liquid Embolic System ("Onyx") was a medical device within the meaning of the FDCA. Onyx is a liquid embolic agent that solidifies upon contact with blood.

10. On or about July 21, 2005, ev3 obtained PMA approval from the FDA to distribute Onyx in the United States for use in the pre-surgical embolization of brain arteriovenous malformations ("BAVMs"). BAVMs are malformed blood vessels located in the brain that result in tangled nests of arteries and veins. BAVMs create weakened arterial structures and problems with blood flow. In the worst cases, BAVMs can cause a vessel to burst, leading to internal bleeding and stroke or death. At all relevant times, the indication for use of Onyx in the United States remained the same.

11. The use of Onyx for its FDA-approved indication in the pre-surgical embolization of BAVMs involved inserting a catheter through a small incision in the groin, navigating the catheter through the body's vasculature to a malformed blood vessel in the brain, and injecting Onyx into the malformed blood vessel through the catheter to stop the flow of blood to the BAVM. The procedure was conducted under fluoroscopy, which allowed the surgeon to view his or her work on a monitor without conducting an open surgery. This type of procedure was called an endovascular procedure and was conducted predominantly by neurointerventional radiologists. The FDA-approved use specified that Onyx was approved for "pre-surgical

embolization" because a surgeon would remove the non-operative vessel and Onyx from the brain in a subsequent open surgery.

12. The FDA-approved labeling for Onyx included a section entitled "Training," which stated: "Serious, including fatal, consequences could result with the use of Onyx LES without adequate training." ev3 developed an extensive training program for surgeons interested in the use of Onyx in the treatment of BAVMs. The training lasted multiple days and included a didactic training session, an animal lab, and physician proctoring of live cases. Each neurointerventional radiologist who wanted to use Onyx for the treatment of BAVMs was required to complete this training prior to the company providing Onyx to the physician.

13. The FDA-approved labeling of Onyx also provided certain warnings, including: "Performing embolization to occlude blood vessels is a high risk procedure. This device should be used only by physicians with neurointerventional training and a thorough knowledge of the pathology to be treated, angiographic techniques, and super-selective embolization."

14. Shortly after the FDA granted PMA approval of Onyx for use in the pre-surgical embolization of BAVMs, ev3 initiated a neurovascular sales and marketing campaign to distribute Onyx to physicians for uses that had not been approved by the FDA.

15. In 2005, as ev3 prepared to begin selling Onyx in the United States, the ev3 Marketing Director directed the company's sales representatives ("territory managers") to seek out surgeons who would use Onyx for surgical procedures outside the brain (known as "peripheral uses" or "peripheral procedures"). Onyx was not approved by the FDA for peripheral procedures and had not been demonstrated safe and effective for such uses. The surgeons who used Onyx for peripheral procedures were predominantly vascular surgeons and interventional radiologists who were not trained to treat BAVMs and whose only use for Onyx was for peripheral procedures, a new use never approved by the FDA.

16. ev3's neurovascular division used a sales incentive structure that compensated territory managers for sales of Onyx for unapproved uses. ev3's neurovascular division also used a sales quota system that set sales targets to include both approved and unapproved uses of Onyx.

17. Consistent with the direction of the Marketing Director and the sales compensation structure, certain ev3 territory managers sought out interventional radiologists and vascular surgeons to encourage them to use Onyx for peripheral procedures. When these surgeons agreed to use Onyx in peripheral procedures, ev3 did not provide them with the type of formal training included in the FDA-approved labeling. Rather, ev3 territory managers often provided only demonstrations or rudimentary training to these surgeons prior to using Onyx in peripheral procedures. ev3 territory managers frequently provided Onyx to the surgeons at the time of surgery for use in peripheral procedures and often also attended the peripheral procedures.

18. On October 22, 2006, an ev3 Regional Manager ("Regional Manager A"), whose area of supervision covered one-third of the country, emailed certain territory managers who worked under his supervision with "Action Items" that included "Close and follow up with all trained, yet unproctored physicians---- no body [*sic*] gets left behind. IR calls should be made in each account to secure endo-leaks, peripheral AVM, etc." The ev3 National Neurovascular Sales Director, who was copied on the email, responded to Regional Manager A, "Very nice coaching . . . The emphasis is clearuly [*sic*] on results – right where we need it." The endo-leak and peripheral AVM procedures referenced in the email that were to be "secured" were both peripheral uses of Onyx that were never approved by the FDA.

19. On November 20, 2006, another Regional Manager ("Regional Manager B"), whose area of supervision covered another one-third of the country, drafted a presentation for

territory managers who worked under his supervision. Under "Activity to achieve to goal," Regional Manager B listed: "Close follow up with all trained, yet unproctored physicians – 'no body [*sic*] gets left behind'. IR calls are to be made in each account to secure endo-leaks, peripheral AVM, etc." This direction was identical to that provided to territory managers in Region A to "secure" unapproved peripheral uses of Onyx.

20. In a June 18, 2008 email, Regional Manager A directed three Territory Managers to make a presentation to other territory managers in the region. In the email, Regional Manager A stated, "At the regional meeting I would like for you to be prepared to present from 11am-12 noon on field Onyx cases 'Peripheral AVM' specifically. The topics I would like you to talk about are as follows: What was successful for me; How did you target and approach the customers; What should TMs look for; What should they watch out for; What are the potential risks or issues." This direction related to an unapproved use ("Peripheral AVM") that was outside of the brain.

21. As ev3 territory managers continued to market, sell, and distribute Onyx to surgeons for peripheral uses, ev3 representatives requested a meeting with FDA to discuss the possible approval of Onyx for use outside the brain. On September 8, 2008, ev3 representatives met with scientists from the FDA to discuss a new potential approval for peripheral use.

22. On September 9, 2008, a physician from the FDA emailed ev3's Regulatory Manager to provide the FDA's view of how ev3 could expand the indication for use of Onyx in the United States. The FDA physician wrote that existing data was inadequate to determine whether the effectiveness of Onyx outweighed the risk for peripheral procedures and that a prospective clinical trial would be necessary to obtain an indication for use in any peripheral procedures. The FDA physician also outlined the FDA's specific safety concerns related to peripheral use of Onyx. He noted that peripheral vasculature could present different approaches

and flow issues that could influence the safety and effectiveness of the device. He also expressed concern that the toxicity of Onyx would present differently in the peripheral vasculature. Finally, the FDA physician emphasized that peripheral use could require significantly larger quantities of Onyx than what had been studied for neurovascular use, thus requiring a study to ensure no new toxicity issues arose at these higher doses.

23. Despite the FDA's expressed concerns regarding unproven use of Onyx in peripheral procedures and despite the FDA's requirement that new clinical data would be necessary for ev3 to obtain approval for such use, ev3 continued the campaign to market, sell, and distribute Onyx for unapproved peripheral use.

24. In October and November 2008, the Onyx Marketing Manager announced a new sales and marketing initiative called Embo Club to the entire ev3 neurovascular sales force. The Marketing Manager instructed territory managers to submit presentations of "interesting" cases, including unapproved peripheral uses of Onyx that would help increase other territory managers' ability to sell more ev3 products. The top presentations would be selected by ev3 marketing and sales managers to be presented to the entire neurovascular sales and marketing team. Two of the first four selected Embo Club presentations touted peripheral uses of Onyx. One of those presentations, singled out for praise by ev3 sales and marketing managers, gave point-by-point instructions for how to work with surgeons to use large quantities of Onyx in a peripheral endo-leak procedure. In that presentation, the territory manager advised his colleagues to consider providing discounts to encourage a surgeon to use large quantities of Onyx for peripheral procedures. The presentation also provided clinical suggestions that the author had given to a surgeon when using Onyx in a peripheral procedure and that he recommended other territory managers provide to surgeons.

25. Consistent with this Embo Club presentation, ev3 territory managers continued to market, sell, and distribute Onyx for use in endo-leaks and other peripheral procedures, none of which were ever approved by the FDA.

26. From on or about August 2005 through on or about December 31, 2009, ev3 was paid at least $6,000,000 for Onyx that was adulterated as defined in 21 U.S.C. §351(f)(1)(B) and introduced into interstate commerce in violation of 21 U.S.C. §§331(a) and 333(a)(1).

COUNT ONE
Introduction of Adulterated Medical Devices into Interstate Commerce
21 U.S.C. §§ 331(a), 333(a)(1)

The United States Attorney re-alleges and incorporates by reference paragraphs 1 to 26 of this Information as if set forth herein, and further charges:

27. From in or about October 2005 to in or about December 2009, in the District of Massachusetts and elsewhere, the defendant

ev3, Inc.

did introduce or deliver for introduction or cause to be introduced or delivered for introduction into interstate commerce the medical device Onyx Liquid Embolic System without a required premarket approval for intended uses outside the brain, rendering the device adulterated under 21 U.S.C. § 351(f)(1)(B), in violation of 21 U.S.C. §§ 331(a) and 333(a)(1), as set forth above.

FORFEITURE ALLEGATION
(18 U.S.C. § 982(a)(7), 28 U.S.C. § 2461(c), and 21 U.S.C. §§ 334 and 853(p))

28. Upon conviction of a violation of 21 U.S.C. §§ 331(a), 333(a)(1), as set forth in Count One of this Information,

ev3, Inc.

the defendant herein, shall forfeit to the United States any property, real or personal, that constitutes or is derived, directly or indirectly, from proceeds traceable to the commission of the offense and all right, title, and interest in any medical device that is adulterated when introduced into or while in interstate commerce or while held for sale after shipment in interstate commerce, or which may not, under the provisions of 21 U.S.C. § 331, be introduced into interstate commerce, pursuant to 18 U.S.C. § 982(a)(7), 21 U.S.C. § 334, and 28 U.S.C. § 2461(c). The property to be forfeited includes, but is not limited to, the following:

a. a forfeiture money judgment in the amount of $6,000,000.00 in United States currency.

29. If any of the property described above as being subject to forfeiture, as a result of any act or omission of the defendant:

b. cannot be located upon exercise of due diligence;

c. has been transferred or sold to, or deposited with, a third party;

d. has been placed beyond the jurisdiction of this Court;

e. has been substantially diminished in value; or

f. has been commingled with other property that cannot be divided without difficulty;

it is the intention of the United States, pursuant to Title 21, United States Code, Section 853(p), as incorporated by Title 28, United States Code, Section 2461(c), to seek forfeiture of any other property of the defendant up to the value of the property described in paragraph 28.

All pursuant to 18 U.S.C. § 982(a)(7), 28 U.S.C. § 2461(c), and 21 U.S.C. §§ 334 and 853(p).

Respectfully submitted,

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